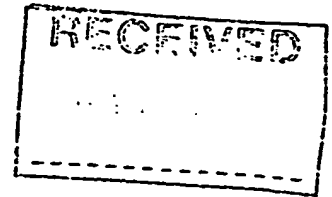
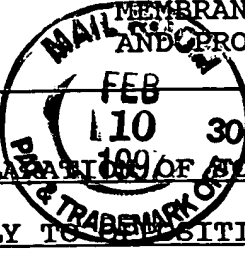


## IN THE EUROPEAN PATENT OFFICE

Applicant : Berman et al.  
European Patent No. : 0 139 417  
Priority Filing Date: August 30, 1983  
For : VACCINES BASED ON  
MEMBRANE BOUND PROTEINS  
AND PROCESS FOR MAKING THEM)



  
DECLARATION OF JOHN K. ROSE IN SUPPORT OF  
REPLY TO OBJECTION BY CHIRON CORPORATION

I, John K. Rose, do declare as follows:

1. I am a citizen of the United States and resident of the State of Connecticut.

2. I received a B.A. with honors in Biology from Brandeis University in Waltham, Massachusetts in 1969, and I received a Ph.D., granted with distinction, in Biology and Biochemical Genetics from Stanford University in Stanford, California in 1973.

3. I have been a professor of Pathology and Cell Biology at the Yale University School of Medicine since 1986. I have been an editor of the journal, Virology, since 1988.

4. The intracellular transport of viral membrane proteins is a primary research interest of mine, and I have authored several journal articles on this subject, including the article printed in Cell 30:753-762 (1982), which I understand was cited by Chiron

Corporation (as Reference J) in their opposition proceedings against the Genentech patent directed to herpes simplex virus vaccines in the European Patent Office.

5. In addition to the journal articles mentioned above, I have published extensively on my research, and I attach as an appendix a list of these publications.

6. I am generally familiar with the subject matter of the above mentioned Genentech patent, European Patent B-0 139 417, and with the work of Laurence Lasky and Phillip Berman relating thereto. I am also familiar with the work reported in the references cited by the opponents, and specifically with the work of Gething and Sambrook, reported in Nature 300:598-603 (1982) (Reference H); the work of Sveda et al, reported in Cell 30:649-656 (1982) (Reference I); and the work of Cohen et al. reported at the Eighth International Herpes virus Workshop, Oxford (July 31, 1983) (Reference L) and at the International Workshop on Herpes viruses in Bologna (1981) (Reference M).

7. To my knowledge, the Genentech researchers, Berman and Lasky, were the first to produce a successful vaccine based essentially on a truncated, membrane-free derivative of a polypeptide expressed from a eukaryotic cell line stably transfected with encoding DNA. In this regard, these researchers used as their model, DNA encoding a truncated, membrane-free glycoprotein D polypeptide of herpes simplex virus to produce a vaccine that successfully raises neutralizing (protective) antibodies against in vivo challenge by a viral pathogen. This subject matter constitutes the scope of the cited European Patent

139,417 as well as their counterpart, scientific publications: Lasky, et al., Bio/Technology 2, 527 (1984) and Berman, et al., Science 227, 1490 (1985).

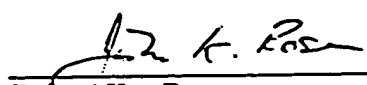
8. Based on my knowledge of the state of the art at the time the invention was first disclosed (August 1983), one of ordinary skill in the art could not have predicted that a successful vaccine that raises neutralizing (protective) antibodies against in vivo challenge by a pathogen could have been produced based essentially on a truncated, membrane-free derivative of a membrane-bound glycoprotein of the virus, produced as an expression product in a eukaryotic cell line stably transfected with encoding DNA.

9. Based upon this pioneering demonstration with the herpes simplex vaccine model, their results provide a reasonable expectation that the system would be successful with other viral pathogens.

10. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, and that willful, false statements may jeopardize the validity of the patent.

Dated: \_\_\_\_\_

12/14/90

  
\_\_\_\_\_  
John K. Rose

DEA-6039  
121390

## CURRICULUM VITAE

**Name:** John Kenneth Rose  
**Date of Birth:** July 21, 1947  
**Place of Birth:** Northampton, Massachusetts  
**Citizenship:** U.S. Soc. Sec. No. 433-68-1751

### Education:

1965-1969 Brandeis University, Waltham, Massachusetts.  
B.A. with honors in Biology  
1969-1973 Stanford University, Stanford, California  
Ph.D. (granted with distinction) in Biology and Biochemical Genetics

### Positions held:

1969-1973 Predoctoral trainee of the U.S. Public Health Service  
with Dr. Charles Yanofsky, Stanford University  
1974-1975 Postdoctoral Fellow, Massachusetts Institute of Technology  
in the laboratories of Drs. David Baltimore and Harvey Lodish  
1976-1978 Research Associate, Massachusetts Institute of Technology  
with Dr. David Baltimore  
1979-1982 Assistant Professor, The Salk Institute  
1982-1986 Associate Professor, The Salk Institute  
1986-present Professor of Pathology and Cell Biology  
Yale University School of Medicine  
1988-present Editor of VIROLOGY

### Research Interests:

Intracellular transport of viral and cellular membrane proteins. Assembly of enveloped viruses. Regulation of viral gene expression.

## Publications:

1. Rose, J.K., Mosteller, R.D. and Yanofsky, C. 1970. Tryptophan messenger RNA elongation rates and steady state levels of tryptophan operon enzymes under various growth conditions. *J. Mol. Biol.* 51:541-550.
2. Mosteller, R.D., Rose, J.K. and Yanofsky, C. 1970. Transcription initiation and degradation of trp mRNA. *Cold Spring Harbor Symp. Quant. Biol.* 35:461-466.
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6. Squires, C.L., Rose, J.K., Yanofsky, C., Yang, H.-L. and Zubay, G. 1973. Tryptophanyl-tRNA and tryptophanyl-tRNA synthetase are not required for *in vitro* repression of the tryptophan operon. *Nature New Biol.* 245:131-133.
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8. Rose, J.K. and Knipe, D. 1975. Nucleotide sequence complexities, molecular weights and poly(A) content of the vesicular stomatitis virus mRNA species. *J. Virol.* 15:994-1003.
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14. Lodish, H.F. and Rose, J.K. 1977. Relative importance of 7-methylguanosine in ribosome binding and translation of vesicular stomatitis virus mRNA in wheat germ and reticulocyte cell-free systems. *J. Biol. Chem.* 252:1181-1188.
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17. Rose, J.K. 1977. Nucleotide sequences of ribosome recognition sites in messenger RNAs of vesicular stomatitis virus. *Proc. Natl. Acad. Sci. USA* 74:3672-3676.
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